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(54) Title: NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(57) Abstract: The present invention provides nucleoside compounds and certain derivatives thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compounds are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compositions containing such nucleoside compounds alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compounds of the present invention.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 05687 A (UNIV BIRMINGHAM ;WELLCOME FOUND (GB); MILLER JOHN ALLEN (GB); YOUN) 17 March 1994 (1994-03-17) abstract page 4	1,12
A	Y. MURAI ET AL.: "A synthesis and an X-ray analysis of 2'-C-, 3'-C- and 5'-C-methylsangivamycins" HETROCYCLES, vol. 33, 1992, pages 391-404, XP008004758 page 391 -page 394	1

☐ Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9405687	A	17-03-1994	AU 4973393 A	29-03-1994
			CA 2143834 A1	17-03-1994
			EP 0658166 A1	21-06-1995
			WO 9405687 A1	17-03-1994
			JP 8504753 T	21-05-1996
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